REMARKS

Status of the Claims

Claims 1, 3-9, and 11-22 are pending in the present application. Claims 2 and 10 were previously canceled. Claims 6, 14, and 18-21 are withdrawn as directed to a non-elected invention. Claims 1, 3, 4, 11, 12, and 18-21 are amended for clarity. Claims 3, 4, 11, and 12 are amended to specify "MHC" class I-restricted, (claims 3 and 11), or "MHC" class II-restricted, (claims 4 and 12), T cell receptor gene. Support for the amendments is found throughout the originally filed application including on page 6 and previously pending claim 1. Claim 22 is new. Support for new claim 22 is found, for example, on page 12, lines 8-9. No new matter is added by way of this amendment. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 3-5, 7, 8, 11-13, and 15-17

Claims 3-5, 7, 8, 11-13, and 15-17 remain rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner believes that the phrases "class I-restricted" or "class II-restricted" are unclear. In response to Applicants' previous argument, the Examiner states that the textbook cited by Applicants refers to **MHC** class I or II-restricted T cell receptor, *emphasis in Office Action.*

In response, the claims are amended to specify "MHC" class I or II-restricted T cell receptor gene. Accordingly, Applicants submit that the claims are not unclear and withdrawal of the rejection is respectfully requested.

Claims 3, 4, 11, and 12

Claims 3, 4, 11, and 12 are also rejected as indefinite for reciting the phrase "by transducing a class I [or class II]-restricted T cell receptor gene." According to the Examiner, it is unclear what is being transduced with the gene for a class I or class II-restricted T cell receptor.

Independent claims 1 and 9 are amended to describe the cells, which are transduced with the specified gene. Accordingly, dependent claims 3, 4, 11, and 12, which incorporate the

features of independent claims 1 or 9, are not indefinite and withdrawal of the rejection is respectfully requested.

Claims 1, 3-5, 7-9, 11-13, and 15-17

Claims 1, 3-5, 7-9, 11-13, and 15-17 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Examiner states that the phrase "by transducing a T cell receptor gene that recognizes a cancer-associated antigen in claims 1 and 9 is unclear. According to the Examiner, it is unclear what is being transduced with the T cell receptor gene.

As noted above, independent claims 1 and 9 are amended to describe the cells that are transduced with the specified gene. Accordingly, Applicants submit that the claims are not indefinite and respectfully request withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103(a)

Claims 1, 3-5, 7-9, 11-13, and 15-17 remain rejected under 35 U.S.C. § 103(a) as allegedly obvious over Tsuji *et al.*, *Cancer*, 2003, 94:389-393, (Tsuji), in view of U.S. Patent No. 7323191 to Gaiger *et al.*, (Gaiger) and Nishimura, *Cancer Treatment and Host*, 2000, 12:363-373, ("Nishimura"). *See* Office Action, pages 5-6.

In response to Applicants' previous argument, the Examiner states that, although Tsuji does not specifically teach using helper T cells for anti-tumor activity, Nishimura teaches that activation of both class II-restricted helper T cells and class I-restricted cytotoxic T cells (CTLs) are important to maximize anti-tumor immunity. Thus, according to the Examiner, one of ordinary skill in the art at the time of the invention would have been motivated to use both helper T cells and CTLs, which are transduced with a T cell receptor gene, for anti-tumor activity.

Applicants submit that an ordinary artisan could not have reasonably predicted at the time of the invention that the same MHC class restricted T cell receptor gene that recognizes a cancer-associated antigen could have been used to obtain both helper cells and cytotoxic T1 cells, which allow for activation of effector functions, since these cells have different signaling requirements.

Applicants further submit that an ordinary artisan recognizes that T cells express T-Cell Receptor (TCR) on the cell surface. The TCR not only recognizes and binds the antigen at its extracellular domain, but also transduces the signal into the cell *via* its intracellular domain.

The TCR of a killer T cell (CTL) is a molecule that recognizes an antigenic substance (cancer-associated antigen) presented on a MHC Class I molecule of a target cell, and transduces (transmits) the signal into the killer T cell, *see* Exhibit A. On the other hand, the TCR of a helper T cell is a molecule that recognizes an antigenic substance presented on a MHC Class II molecule of a monocyte/macrophage, and transduces the signal into the helper T cell, *see* Exhibit B.

In view of the foregoing, a helper T cell and a killer T cell receive signals from different (respective) molecules, utilize different mechanisms of signal transduction, and exert different (respective) functions. In other words, a specific combination of TCR (signal inlet) and signal transduction mechanism is required in each of these cells types to allow each cell to exert its respective function.

The Office Action alleges that at the time of the invention, it would have been obvious to an ordinary artisan to replace the combination of cells and TCRs disclosed in Tsuji or in Nishimura with Th cells transduced with the TCR gene that recognizes a cancer-associated antigen, as described in the present claims, to induce CTL. Accordingly, the Office Action indicates that an ordinary artisan would have conceived of replacing the TCR to alter the function of cells. Applicants submit that this allegation is incorrect.

At the time of the invention, an ordinary artisan was well-aware of the signal transduction mechanisms of Th cells and killer T cells as described above, and would have, accordingly, reasonably expected that a cell, transduced with the TCR gene described in the instant claims, would not have functioned properly because the cell would have lacked the essential signal transducing molecules downstream of the TCR.

In other words, an ordinary artisan would have reasonably understood that, even if the signal inlet is replaced, the signal would not be transmitted because the downstream mechanisms within the cells are not adapted, and thus, the cellar function would not be altered (the cells cannot exert the desired function).

The method of the present invention is characterized by imparting antigen specificity to a helper T cell by transducing a TCR gene that recognizes a cancer-associated antigen to the helper T cell. As discussed above, such a feature would not have been reasonably predicted from the knowledge in the art at the time of the invention and an ordinary artisan could not have reasonably expected that the instant invention could have been achieved.

In view of the foregoing, the instant claims are not obvious over the cited references. Withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should there by an outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: MAR 0 9 2010

Respectfully submitted,

By _____
Gerald M. Murphy, Jr.
Registration No.: 28977
BIRCH, STEWART, KOLASCH & BIRCH, LLP
8110 Gatehouse Road, Suite 100 East
P.O. Box 747
Falls Church, VA 22040-0747
703-205-8000

Attachments: Exhibit A
Exhibit B

Exhibit A

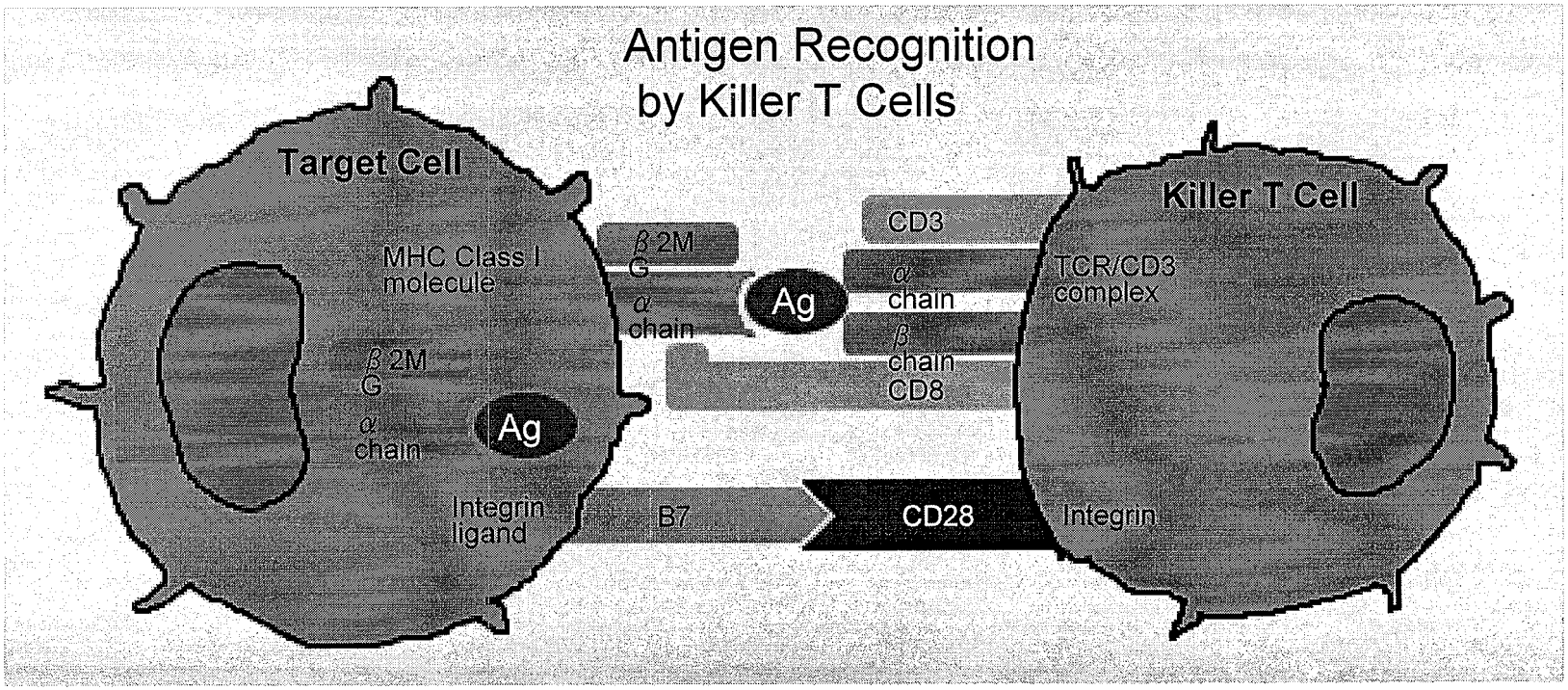
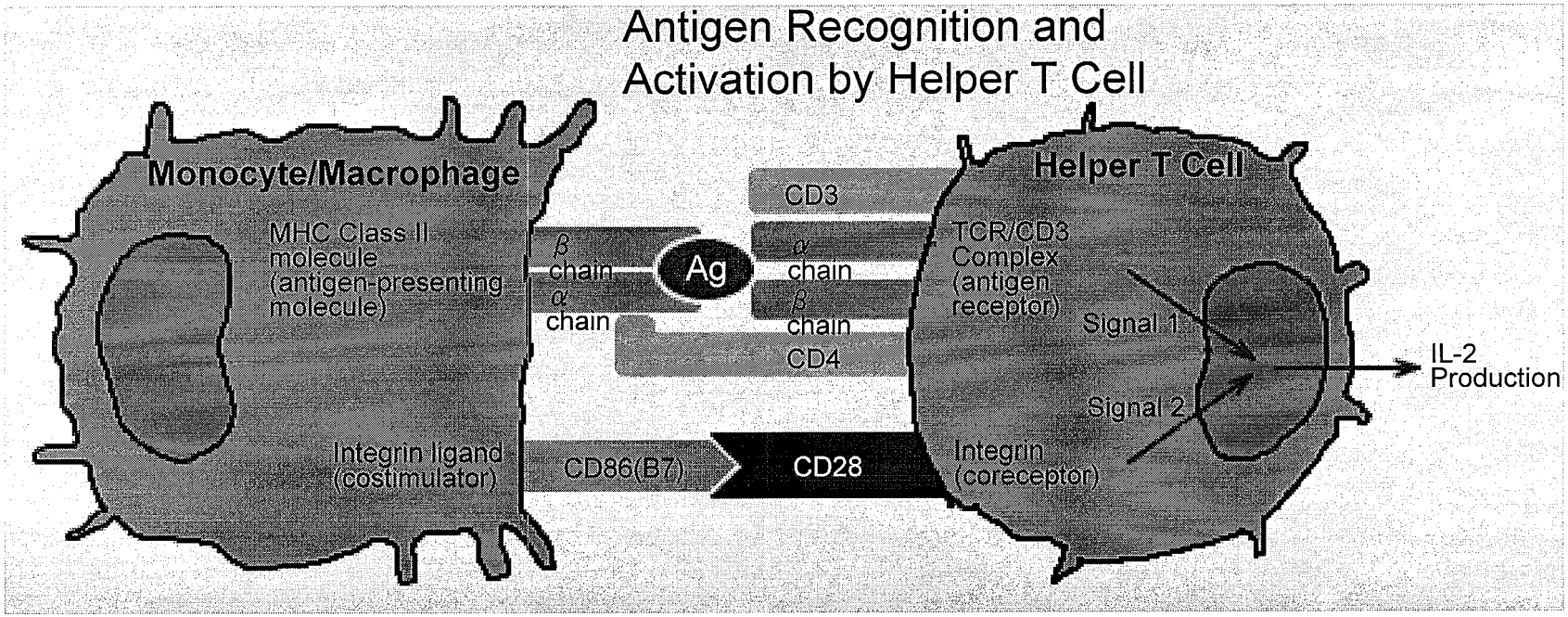

Antigen Recognition
by Killer T Cells
Target Cell
MHC Class I
molecule
β 2M
G
α
chain
Ag
Integrin
ligand
β 2M
G
α
chain
Ag
CD3
α
chain
β
chain
CD8
B7
CD28
Killer T Cell
TCR/CD3
complex
Integrin

Exhibit B


Antigen Recognition and
Activation by Helper T Cell
Monocyte/Macrophage
MHC Class II
molecule
(antigen-presenting
molecule)
β
chain
α
chain
Ag
CD3
α
chain
β
chain
CD4
Helper T Cell
TCR/CD3
Complex
(antigen
receptor)
Signal 1
IL-2
Production
Signal 2
Integrin ligand
(costimulator)
CD86(B7)
CD28
Integrin
(coreceptor)